Remarks

Claims 1-24 are pending in this application. The Applicants amend in this paper claims 1 and 7 and withdraw in response to a restriction requirement claims 2-6; the Applicants withdrew claims 8-16, also in response to a restriction requirement, in a previous paper.

The Examiner objected that claims 1 and 7 recite non-elected SEQ ID NOS., and objected to claims 17-20 in so far as they depend on claim 1. The Applicants have amended claims 1 and 7 such that they recite only SEQ ID NO:1. The Applicants respectfully request, therefore, that the Examiner withdraw the objection as to these claims.

The Examiner rejected claims 1, 17, and 17-24 under 35 U.S.C. §§ 101 and 112, first paragraph, stating that the claims are not supported by a specific and substantial asserted utility or a well established utility. The Examiner stated that "there is no physiological or biological significance attached to the claimed nucleic acid or the encoded protein." The Applicants respectfully disagree.

The protein encoded by the sequence of SEQ ID NO:1 has an important role in the resistance to nucleotide analogs. *See* the specification at, for example, ¶¶ 5, 6, and 8. A recent paper by Y. Guo *et al.* (J. Biol. Chem., 278, 29509-19514 (2003)), submitted with this Amendment, confirms this function.

Guo *et al.* establish that the nucleotide of SEQ ID NO:1 – the Applicants refer to it as ABCC11, Guo *et al.* refer to it as MRP8 – has a credible, specific, and substantial utility, namely, that MRP8 is a factor in drug resistance to fluoropyrimidines. *See* Guo *et al.* at 29509, second paragraph, and 29513, fourth full paragraph ("Analysis of the drug sensitivity of MRP8-transfected LLC-PK1 cells showed that MRP8 is able to confer resistance to fluoropyrimidines, ddC, and PMEA."). This is not merely a substantial real-world utility, but an important one, because the fluoropyrimidines are the most frequently used chemotherapies in the treatment of colon, breast, and head and neck cancers:

> Fluoropyrimidines, which are a mainstay in the treatment of colon cancer and are also active in breast and head and neck cancer, are among the most widely employed anticancer agents.

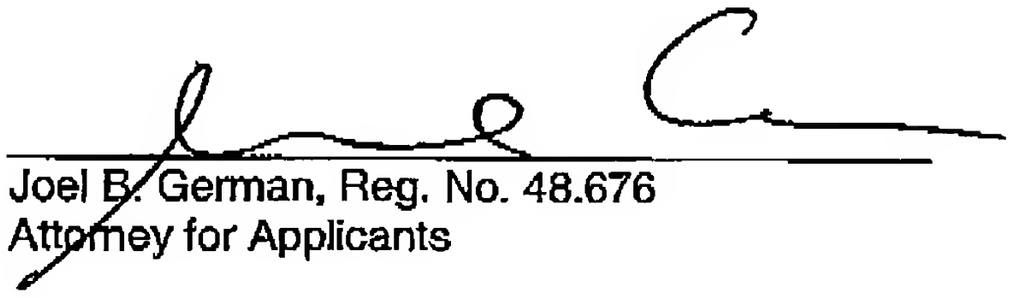
Id., at 29509, fourth full paragraph. In addition to this significant utility, MRP8 also has the ability to confer resistance to ddC, an anti-AIDS drug. *Id.*, at 29509, fourth full paragraph, and 29514.

Guo *et al.*'s work suggests that MRP8 is a lipophilic anion pump, which functions to extrude cyclic nucleotides. The authors note that "numerous types of mammalian cells" have the ability to extrude cyclic nucleotides, and that this ability is "well documented" and "well established," so their results are not surprising. *See* Guo *et al.* at 29513, first and second full paragraphs. The utility that Applicants assert – that the sequence of SEQ ID NO:1 encodes a protein which is a marker for resistance to one of the most important types of cancer drugs – is therefore credible, because it associated with a cellular mechanism that is "well documented" and "well established."

In view of the foregoing, the Applicants respectfully submit that the claims define an invention with a substantial, credible, and specific utility, and respectfully request that the Examiner withdraw the rejection under §§ 101 and 112, first paragraph and withdraw the finality of the Office Action. In the alternative, the Applicants request that the Examiner enter this Amendment so as to place the claims in better condition for appeal.

The Applicants respectfully submit that the claims, as amended, are in condition for allowance, and respectfully request early, favorable action on the application. Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite her to contact the undersigned at 908.231.3444.

Respectfully submitted,



Joel B. German, Reg. No. 48.676
Attorney for Applicants

Aventis Pharmaceuticals Inc.
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-3444
Telefax (908) 231-2626
Aventis Docket No. ST01005 US NP